

## REMARKS

The Office action dated June 4, 2009 is acknowledged. Claims 1-22 are pending in the instant application. According to the Office action, claims 1-9, 13-15, 18 and 19 have been rejected and claims 10-12, 16, 17 & 20-22 have been withdrawn. Claims 1-3, 6, 7 and 18 have been amended. Claims 5 and 9 have been canceled. Claims 23-27 have been added to more clearly define the present invention, support for which may be found throughout the specification.

Claim 1 has been amended to more precisely define the backing layer as comprising at least one “neutralized polymethyl methacrylate.” Support can be found in claim 5, now canceled herewith. The term “layer” was also deleted, as supported by the specification, page 5, last two lines – page 6, line 1.

Claim 1 has also been amended to more clearly define the function and position of the backing layer. The term “a boundary layer for reducing the permeation of water and the diffusion of active substance, relative to the other layer(s) of said system” has been added thereto. Support can be found in claim 9, now canceled herewith.

Claim 1 has been further amended to recite that the mucoadhesive polymer is selected from the group consisting of polyacrylates and salts of polyacrylates, as supported by claim 3 (the limitation having been deleted from that claim herewith). In addition, claim 1 is amended to indicate that the mucoadhesive layer also contains active substance(s), as supported in the specification. Accordingly, the phrase “at least one of said at least two layers of said system contains an active substance” has been deleted therefrom.

New claims 23-26 are supported by the deleted portions of present claim 6.

New claim 27 is identical to claim 1, except that the polyacrylate of the backing layer is not limited to “neutralized polymethyl methacrylate.”

Reconsideration is respectfully requested in light of the amendments being made hereby and the arguments made herein. No new matter has been added.

**Oath/Declaration**

The issue regarding the oath/declaration has been resolved by the prior response filed on August 18, 2009. Withdrawal of the rejection is thus requested.

**Rejection of Claims 2, 7 and 18 under 35 U.S.C. 112, second paragraph**

Claim 2 has been rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation “substantially comprises.” Claim 2 has been amended accordingly.

Claims 7 and 18 were rejected as being indefinite in their recitation of “chemically allied.” These claims have been amended accordingly.

Withdrawal of these rejections is thus requested.

**Rejection of Claims 1-9, 13-15, 18 and 19 under double patenting**

Claims 1-9, 13-15, 18 and 19 have been provisionally rejected under the obviousness-type double patenting doctrine as being unpatentable over claims 1-4 and 7-9 of co-pending Application No. 11/408,958 in view of Rault, et al. and Ruprecht (both discussed below). The Examiner argues that the present claims are not patentably distinct from those of ‘958 because the scope of the ‘958 claims renders obvious that of the instant claims. The Examiner states that the difference between the two claim sets is that the ‘958 claims recite rapid release from one layer and slow release from another layer. However, the Examiner’s position is that this element – and thus the entire scope of the

instant claims – is rendered obvious since the instant claim 14 recites at least two layers containing an active substance at different concentrations.

On page 17 of the Office action and noted above, the Examiner states that “the difference between the two claim sets is that the ‘958 claims recite rapid release from one layer and slow release from another layer.” In this case, rapid release is produced by employing a layer which is capable of rapidly dissolving in aqueous surroundings (see, for example, U.S. Published App. No. 2006/0198878, paragraph [0016]). In contrast, the present claims pertain to a film-shaped therapeutic system which has mucoadhesive properties due to the presence of a mucoadhesive layer that swells in an aqueous medium, but is insoluble or poorly soluble in the aqueous medium.

Therefore, regarding obviousness, the question appears to be whether the skilled person would have considered modifying the invention defined in the co-pending claims to obtain mucoadhesive films as presently claimed. With the film-shaped preparations claimed in the co-pending application, a bi-phasic release pattern (i.e., rapid-slow) is observed when the preparations are eroded from both sides, i.e., when the surface of the rapidly-releasing layer and the surface of the slowly-releasing layer are exposed to the surrounding aqueous medium (see, for example, U.S. Published App. No. 2006/0198878, paragraphs [0068] – [0070]). Therefore, according to the teaching of the co-pending application, it is essential that both layers/surfaces are exposed to the surrounding medium so that a bi-phasic release can be achieved. Therefore, based on this teaching, the skilled person would not have considered changing the compositions of the fast/slow release layers to render one of these layers mucoadhesive, since such modification would

be expected to be incompatible with the requirement of producing a bi-phasic release pattern discussed therein.

In conclusion, the Applicant respectfully disagrees with the Examiner's statement that the instant claims represent an obvious variation of the '958 claims. In addition, while the Examiner has generally referred to Rault and Rupprecht, no specific reasons were indicated to support the notion that the present claims would be directed to an invention that is not patentably distinct from the claims of the '958 application. Withdrawal of the obviousness-type double patenting rejection is requested.

**Rejection of Claims 1-9, 13-15, 18 and 19 under 35 U.S.C. 103(a)**

Claims 1-3, 7-9 and 19 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 4,740,365 (Yukimatsu, et al.). The Examiner argues that Yukimatsu, et al. teach a two-layer sustained release preparation for application to mucous membranes in the oral cavity and that the preparations have a film-like shape. The Examiner also states that Yukimatsu, et al. teach that a first layer comprises an active ingredient and one or more polymers including polyvinyl alcohol and a copolymer of maleic anhydride and methyl vinyl ether. The Examiner further states that Yukimatsu, et al. teach that a second layer (i.e., a backing layer) comprises one or more polyacrylic acid (i.e., polyacrylate) polymers. Thus, the Examiner concludes that Yukimatsu, et al. teach every limitation of claim 1 except that the Yukimatsu, et al. does not embody the claimed invention sufficiently to be anticipatory.

Claims 4-6, 13-15 and 18 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Yukimatsu, et al. and further in view of WO 01/03917 (Rupprecht). The Examiner argues that Yukimatsu, et al. teach the limitations of these claims. The

Examiner also states that one skilled in the art would be motivated to select cross-linked polymers for the mucoadhesive layer in light of Rupprecht. The Examiner further states that Rupprecht discloses transmucosal multi-layered films made of film-forming polymers and that the ratio of cross-linking agent (i.e., the amount of crosslinking) may be varied to optimize the film properties such as the active substance release properties of the film. The Examiner thus concludes that it would have been obvious to select a cross-linked polymer as taught by Yukimatsu, et al. with the motivation of high expectation of success since Yukimatsu, et al. teach the use of cross linked polymers in either of the two layers and since Rupprecht teaches that the amount of cross-linking can be adjusted to optimize the release properties of the film.

Claims 1-9, 13-15, 18 and 19 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,242,004 (Rault, et al.) in view of Rupprecht. The Examiner argues that Rault, et al. teach multilayered bioadhesive compounds for transmucosal administration of active substances and that the compositions are tablets that have a flat or oblong shape (i.e., film-shaped). The Examiner also argues that Rault, et al. disclose the multilayered bioadhesive compounds for transmucosal administration of active substances and that the compositions are tablets that have a flat or oblong shape (i.e., film-shaped) to ensure the best prolonged maintenance of the form on its site of action. The Examiner also states in the Office action that the reference teaches all other limitations of these claims, except that Rault, et al. do not embody the specific combination of the exact polymer species claimed in the invention sufficiently to be considered anticipatory.

The Examiner refers to Rupprecht for disclosing transmucosal multi-layered films made of film-forming polymers. The Examiner also states that Rupprecht teaches that preferred cover (i.e., backing) layer materials are films formed from mixtures of polymers and teaches that Eudragit E (i.e., a neutralized polymethyl methacrylate) is a suitable preferred cover layer material and that mixtures of polymers may be used in the backing layer to optimize the properties of this layer, which Rupprecht teaches include mechanical stabilization of the film, diffusion prevention of the active substance, unidirectional release of the active substance and adjustment of the sustained release profile of the active agent. The Examiner thus concludes that it would have been obvious to one skilled in the art to use polyacrylates in the backing layer with motivation being the high expectation of success since Rault, et al. teach the use of polyacrylates and since Rupprecht teaches that polyacrylates are preferred base polymers for the backing layer.

The Applicant respectfully submits that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitation. The Applicants respectfully submit that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider the combined teachings of the prior art, each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success if the aforementioned references were to be considered.

The Applicant respectfully disagrees with the Examiner's conclusion set forth in the Office action and summarized above. In the two-layer preparation described in Yukimatsu, et al. (col. 3, lines 22-54), layer (I) does not contain a neutralized polymethyl methacrylate, as recited in present claim 1, or at least one polyacrylate, as recited in new claim 27. Therefore, based on this prior art teaching, it would not have been obvious to include neutralized polymethyl methacrylates into the backing layer of an at least two-layered preparation.

In this regard, the Examiner notes on page 7 of the Office action that "Yukimatsu teaches a second layer ... comprises one or more polyacrylic acid (i.e., polyacrylate)." However, contrary to the Examiner's suggestion, Yukimatsu, et al. do not equate polyacrylic acid with polyacrylate. The terms "polyacrylic acid" and "polyacrylate" refer to two different classes of polymers. Polyacrylic acids are polymers obtained by polymerization of *acrylic acid*, whereas polyacrylates are polymers based on *esters of acrylic acid*. The enclosed copies from "Rompp Chemie Lexikon" (Rompp Chemical Encyclopedia), 9<sup>th</sup> Edition, pp. 3506-3508 are referenced for supporting this. As can be seen from the general formulas, the acrylic acid is esterified (-COOR) in the case of polyacrylates. The fact that there are two separate entries for "polyacrylates" and "polyacrylic acid" is a strong indication that these two polymer classes are generally regarded as being different from each other. Therefore, the Applicants respectfully submit that the Examiner's suggestion "polyacrylic acid (i.e., polyacrylate)" appears to be incorrect.

The Applicant also disagrees with the rejection of the present claims over Yukimatsu, et al. in view of Rupprecht. Rupprecht fails to make up for any of the

aforementioned deficiencies of Yukimatsu, et al. Rupprecht teaches a backing layer (cover layer) which may be produced from polyacrylates or, in particular, neutralized polymethyl methacrylate. This backing layer is distinguished from layer (I) of Yukimatsu, et al. in that it does not appear to contain any active substance. Hence, since layer (I) of Yukimatsu, et al. serves a different purpose and, in turn, must have different properties as an active substance-containing layer, it would not be obvious to modify layer (I) of Yukimatsu, et al. by incorporating polyacrylates or, in particular, neutralized polymethyl methacrylate of Rupprecht since such polymers are taught by Rupprecht specifically in connection with a backing layer that does not contain an active substance. One skilled in the art would not have had any motivation to combine the teachings of Rupprecht with Yukimatsu, et al.

Furthermore, regarding the mucoadhesive layer, it is noted that according to present claim 1, this layer is composed of (at least) two different polymer components. The matrix of this layer is formed by polyvinyl alcohol, and it contains mucoadhesive polymers (polyacrylates) dispersed therein. In contrast, the active substance-containing layer taught by Rupprecht does not contain polyvinyl alcohol. While it is true that layer (I) of Yukimatsu, et al. can comprise polyvinyl alcohol, Yukimatsu, et al. fail to teach that this layer comprises polyacrylates. It is also noted that Yukimatsu, et al.'s layer (II) does not contain polyacrylates, for the same reasons discussed at length above.

Due to the reasons set forth above, it would not have been obvious for one skilled in the art to include neutralized polymethyl methacrylate in an active substance-containing backing layer of an at least two-layer system, and to include polyacrylates in a matrix formed of polyvinyl alcohol to obtain a mucoadhesive layer.

The Applicant also disagrees with the Examiner's conclusion that the claimed invention would be obvious over Rault, in view of Rupprecht. Rault relates to tablets which are clearly different from film-shaped systems, as presently claimed. One skilled in the art would readily recognize that a tablet is an administration form which is fundamentally different from an administration form that is characterized as being film-shaped.

According to the Examiner at page 16 of the Office action, it would have been obvious to use polyacrylates in the backing layer as taught by Rault since Rupprecht teaches neutralized polymethyl methacrylates for this purpose. However, as noted above, Rupprecht's backing layer does not contain active substance and, therefore, it would not be obvious to include such polymers in an active substance-containing layer. Rupprecht fails to make up for any of Rault's deficiencies.

It is therefore respectfully submitted that the present invention defined in the present claims is patentably distinguishable over the combination of prior art teachings under 35 U.S.C. 103(a). Based on the aforementioned differences, each and every element of the present invention recited in the present claims are not set forth in the prior art. Moreover, one skilled in the art would not be motivated to combine the teachings of the prior art references to arrive at the presently claimed invention. Therefore, the Applicant respectfully requests that this rejection be withdrawn.

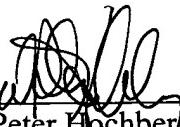
### **Conclusion**

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art

references, the Applicant strongly urges that the obviousness-type rejection and anticipation rejection be withdrawn. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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